REMARKS

1. Preliminary Remarks

a. Status of the Claims

Claims 1-23 are pending in the application, of which claims 1-23 are under active consideration. Claims 1, 6-9, 11-13, 16, 18, 22 and 23 are amended. Claims 24 is new. Claims 2-5, 14-15 and 19-21 are canceled. Applicant respectfully requests entry of the remarks and amendments made herein into the file history of the application. Upon entry of the amendments, claims 1, 6-13, 16-18 and 22-24 will be pending, of which claims 1, 6-13, 16-18 and 22-24 will be under active consideration.

b. Claim Amendments

Claim 1 is amended to incorporate the definitions of A, B and Y from claim 3 and to recite "di-(C_1-C_4-alkyl)amino". Claims 1, 6-9, 11-13 and 18 are amended to recite "formula" in place of "general formula". Claims 1 and 18 are amended to recite "N-oxides of formula I" and claim 18 is amended to recite "salts of formula I". Claims 7 and 11 are amended to recite "as claimed in claim 1" in place of "in the abovementioned manner". Claim 8 is amended to recite the variable "NR^3" instead of the variable "Y" to reflect the incorporation of claim 3 into claim 1. Claim 12 is amended to remove and unintended second occurrence of "or C_1-C_4-alkoxy, C_1-C_4-alkylamino, di-(C_1-C_4-alkyl)amino, phenyl, phenoxy, C_3-C_8-cycloalkyl and C_3-C_8-cycloalkyloxy, where the last four groups mentioned may optionally have one or more substituents selected from C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy and halogen" in the definition of the substituents on R^{1a}. Claim 13 is amended to depend on claim 12. Claim 16 is amended to depend on claim 1. Support for these amendments can be found throughout the specification and claims as originally filed. Claim 22 is amended to recite "wherein the medical disorder is selected from the group consisting of schizophrenia, depression, parkinsonism, and renal function disorders" Claim 23 is amended to recite a disorder "selected from the group consisting of schizophrenia, depression and parkinsonism." Claim 24 is new. Support for these amendments and new claim can be found at least on page 25, line 27 to page 26, line 15 and page 27, line 35 to page 28, line 2 of the specification.

c. Claim Objections

On page 15 of the Office Action, the Examiner objects to claim 14 under 37 C.F.R. § 1.75(c) as allegedly being in improper form because a multiple dependent claim must be in the alternative. Claim 14 has been canceled. In view of the foregoing, Applicant respectfully submits that the

Examiner's objection to claim 14 under 37 C.F.R. § 1.75(c) as allegedly being in improper form is overcome and requests withdrawal of the same.

2. Patentability Remarks

a. 35 U.S.C. § 112, first paragraph

On pages 2-4 of the Office Action, the Examiner rejects claims 19-23 under 35 U.S.C. § 112, first paragraph, for allegedly lacking enabling support from the specification. The Examiner asserts that the specification does not enable one of skill without undue experimentation to treat disorders of the central nervous system susceptible to treatment with dopamine D3 receptor antagonists. Applicant respectfully disagrees.

Nevertheless, in order to expedite prosecution and without prejudice to seeking broader claims in a continuing application, claims 19-21 have been canceled and claims 22 and 23 have been amended. Amended claims 22 and 23 now relate to treating schizophrenia, depression, parkinsonism, and renal function disorders.

The basis for the Examiner's enablement rejection is that former claims 22 related to treating any and all diseases and/or conditions associated with the modulation of the dopamine D_3 receptor antagonists, agonists and ligands. Amended claims 22 and 23, however, no longer embrace any and all diseases and/or conditions associated with the modulation of the dopamine D_3 receptor antagonists, agonists and ligands, but instead are not limited to treating the particular conditions of schizophrenia, depression, parkinsonism, and renal function disorders. Applicant submits that treating these conditions is enabled because researchers have recognized that each of these conditions is amenable to treatment by modulating D_3 receptor activity, that those of skill knew how to use compounds to modulate D_3 receptor activity, and thus no undue experimentation was necessary to use the instantly claimed compound, which is described in the instant application, for these treatments. (See also MPEP §2164.01)

Researchers have recognized the use of D_3 receptor antagonists to treat Parkinson's Disease (PD). Specifically, the literature states that "elevations of the D_3 receptor occur in schizophrenia and in experimental conditions of hyperdopaminergic tone… which also may occur with L-dopa-induced dyskinesias in PD. Thus, D_3 receptor antagonists could prove to be effective in the treatment of schizophrenia…," further that, "[an] effective antiparkinsonian D_3-preffering agonist… [exhibits] antidepressive effects" and even further that, "**experimental models of PD suggest that D_3-preferring agonists do act through D_3 receptors to provide relief of akinesia**." J.N. Joyce. Pharmacology and Therapeutics, 2001;90:231-59 at pages 251-2 (emphasis added). Accordingly,

researchers recognized that dopamine D_3 receptor-targeting drugs could be used to treat disorders including PD, schizophrenia, depression, and others. Additionally, D_3 receptors have been implicated in regulating renal function. *See* Mühlbauer *et al.*, Acta Physiologica Scandinavica, 2000;168(1):219-23. These references indicate that the evidentiary connection between the instantly claimed compounds and their potential use for treating PD, schizophrenia, depression and renal function disorders was sufficiently studied and would be convincing to one of skill in the art regarding how the claimed compound might be used to treat the conditions claimed in amended claims 22 and 23. Applicant respectfully submits this evidence merely needs to be convincing rather than conclusive to one of skill in the art. *See* MPEP § 2164.05 and In re Brandstadter 482 F.2d. 1935 (CCPA 1973).

Further, the instant application discloses that the instantly claimed compounds modulate dopamine D_3 receptor activity, and have considerable bioavailablility in the plasma and the brain. Based on the instant written description and in view of the teaching of the art described above, Applicant submits that the scope of amended claims 22 and 23 are sufficiently enabled by the instant written description because one of ordinary skill in the art could readily have anticipated the effects of a change within the claimed subject matter without further undue experimentation. *See* MPEP §§ 2164.01 and 2164.03.

Although some experimentation might have been necessary to establish the extent of the usefulness of the instantly claimed compounds, the instantly claimed subject matter was enabled because one of ordinary skill in the art had sufficient direction and guidance from the instant written description as to how to use the compound to treat the conditions of amended claimed 22 and 23 - determining the extent to which the instantly claimed compounds treat these conditions was routine, as demonstrated by the references described above. *See* MPEP § 2164.05. In view of the foregoing amendments and remarks, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement.

b. 35 U.S.C. § 112, second paragraph

On pages 4-8 of the Office Action, the Examiner rejects claims 1-23 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Specifically, the Examiner alleges that claims 1-9, 11-14, 18 and 19 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "general" formula I.

Claims 1-9, 11-14, 18 and 19 have been amended to remove all instances of "general" and now properly refer to formula I.

The Examiner alleges that claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "Di-(C_1-C_4-alkyl)amino" in the definition of the substituents of R^1. Claim 1 has been amended to recite "di-(C_1-C_4-alkyl)amino" in the definition of the substituents of R^1 thereby clarifying the member of the R^1 substituent group. The Examiner further alleges that claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "R^4-R^8", which is a range which does not particularly point out and distinctly claim the subject matter which applicants regard as the invention. Claim 1 has been amended to recite "R^4, R^5, R^6, R^7, and R^8" thereby clarifying all the substituent groups defined in "R^4-R^8".

The Examiner alleges that claim 1 and 18 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "the N-oxides of I" at the end of the claim. Claims 1 and 18 have been amended to recite "the N-oxides of formula I" at the end of the claim.

The Examiner alleges that claims 7 and 11 are vague and indefinite in that it is not known what is meant by "the abovementioned manner." Claims 7 and 11 are amended to recite "as claimed in claim 1."

The Examiner alleges that claim 12 is vague and indefinite in that it is not known what is meant by the second occurrence of "or C_1-C_4-alkoxy, C_1-C_4-alkylamino, di-(C_1-C_4-alkyl)amino, phenyl, phenoxy, C_3-C_8-cycloalkyl and C_3-C_8-cycloalkyloxy, where the last four groups mentioned may optionally have one or more substituents selected from C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy and halogen" in the definition of the substituents on R^{1a}. Claim 12 has been amended to remove this second occurrence.

The Examiner alleges that claim 13 has insufficient antecedent basis for the limitation "R^{1a}" in the second line. Claim 13 has been amended to depend on claim 12, which provides a proper antecedent basis for the limitation "R^{1a}".

The Examiner alleges that claim 14 is vague and indefinite in that it is not known what is meant by the formula label (1.A/B) and 1.A. The Examiner further alleges that claim 14 has insufficient antecedent basis for the limitation "R^{1a}" in the 6th and 8th lines. Claim 14 is canceled thereby rendering these rejections moot.

The Examiner alleges that claim 18 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "the salts of I" in line 3 of the claim. Claim 18 has been amended to recite "the salts of formula I" in line 3 of the claim.

The Examiner alleges that claims 19-22 are vague and indefinite in that the claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in determining which are the diseases capable of being mediated by a dopamine D_3 receptor antagonists or agonists or a dopamine D_3 receptor ligand. Claims 19-21 have been canceled. Claim 22 has been amended to identify the diseases capable of being mediated by a dopamine D_3 receptor ligand, namely schizophrenia, depression, parkinsonism, and renal function disorders.

The Examiner alleges that claims 19-21 are indefinite for reciting a use without any active, positive steps delimiting how the use is actually practiced. Claims 19-21 have been canceled.

In view of the foregoing, Applicant respectfully submits that the rejection of claims 1-23 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention is overcome and requests withdrawal of the same.

c. 35 U.S.C. § 101

On page 9 of the Office Action, the Examiner rejects claims 19-21 under 35 U.S.C. § 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e. results in a claim which is not a proper process claim under 35 U.S.C. § 101. Claims 19-21 have been canceled thereby rendering the rejection moot. In view of the foregoing, Applicant respectfully submits that the Examiner's rejection of claims 19-21 under 35 U.S.C. § 101 is overcome and requests withdrawal of the same.

d. 35 U.S.C. § 102(e)

On pages 9-10 of the Office Action, the Examiner rejects claims 1, 2, 6-10 and 12-23 under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent Application Pub. No. 2005/0085461 ("Cooper"). On page 10 of the Office Action, the Examiner rejects claims 1, 2, 6-9, 11-13 and 15-23 under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent Application Pub. No. 2005/0090485 ("'485"). On pages 10-11 of the Office Action, the Examiner rejects claims 1, 2, 6-8, 12, 13 and 15-23 under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent Application Pub. No. 2005/0222124 ("'124"). Applicant respectfully traverses these rejections.

Cooper, '485 and '124 disclose aryl sulfonamides of 7-aminobenzazepine compounds. Aryl sulfonamides of 7-aminobenzazepines, however, are no longer covered by instant claim 1 because such compounds would require that each of the Y and A in formula I of originally filed claim 1 are a single bond and the group B is a group NR^3. Amended claim 1 does not provide such a possibility and therefore Cooper, '485 and '124 do not anticipate the instantly claimed subject matter. In view

of the foregoing, Applicant respectfully submits that the rejection of claims 1,2, 6-10 and 12-23 under 35 U.S.C. § 102(e) as allegedly being anticipated by Cooper, the rejection of claims 1, 2, 6-9, 11-13 and 15-23 under 35 U.S.C. § 102(e) as allegedly being anticipated by '485, and the rejection of claims 1, 2, 6-8, 12, 13 and 15-23 under 35 U.S.C. § 102(e) as allegedly being anticipated by '124 are each overcome and requests withdrawal of the same.

e. 35 U.S.C. § 103(a)

On pages 11-12 of the Office Action, the Examiner rejects claims 1, 2, 6-10 and 12-23 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Cooper. On pages 12-14 of the Office Action, the Examiner rejects claims 1, 2, 6-13 and 15-23 under 35 U.S.C. § 103(a) as allegedly being unpatentable over '485. On pages 14-15 of the Office Action, the Examiner rejects claims 1, 2, 6-8, 12, 13 and 15-23 under 35 U.S.C. § 103(a) as allegedly being unpatentable over '124. Applicant respectfully traverses these rejections.

As discussed above, the compounds disclosed in Cooper, '485 and '124 do not fall within the scope of amended claim 1 because they contain an arylsulfonamide radical. The instantly claimed compounds contain an arylsulfonyl radical and cannot contain an arylsulfonamide radical. The Examiner has pointed to no teaching or suggestion within Cooper, '485 or '124 that would motivate the skilled artisan to sufficiently alter the arylsulfonamide radical of Cooper, '485 or '124 to arrive at the arylsulfonyl of the instantly claimed compounds.

In this instance, altering the arylsulfonamide radical to an arylsulfonyl radical would be expected to disturb the biological activity of the starting compounds, namely compounds of formulas I of Cooper, '485 and '124. Specifically, Applicant submits that the skilled artisan is well aware that altering the distance between molecular moieties and removing an amine group will change the shape of the molecule and thus its binding properties.

Even if the skilled artisan were somehow motivated, among all the possible options, to modify the arylsulfonamide radical, said artisan would be altering an apparently critical aspect of the starting molecule, namely the arylsulfonamide radical. Cooper discloses compounds where the arylsulfonamide radical is maintained, **identically**, for all 9 example compounds and all 82 compounds of Tables 1, 2 and 3 as well as the claims. '485 discloses 17 example compounds with biological activity at the 5-HT_6 receptor and all of the claims disclose compounds where the arylsulfonamide radical is maintained, **identically**, for all 17 example compounds. The '124 patent discloses compounds where the arylsulfonamide radical is identical across 217 compounds in examples 1-10, 42-45, 107, 216-217 and 210, the claims, Tables 1, 2 and 3, and the claimed

invention. Furthermore, all of the claims of Cooper, '485 and '124 are drawn to compositions and methods for using compositions containing the identical arylsulfonamide radical. Consequentially, Applicant submits that even if Cooper, '485 and '124 provided a motivation to modify the disclosed compounds - which they do not - the skilled artisan would not act in direct contravention of the reference's teaching by modifying a substituent group implied as critical for biological activity in order to solve the problem of identifying molecules with biological activity at the dopamine D_3 receptor.

Cooper, '485 and '124 also fail to disclose any structure activity relationships that could provide an expectation of success in modifying the compounds from Cooper, '485 or '124 to retain biological activity. Applicant submits that in the field of drug design, in the absence of a known connection between the structure of a compound and its function, any structural modification to a pharmaceutically active compound would *a priori* be expected to disturb the pharmacological activity profile of the initial structure. Accordingly, the skilled artisan would not have a reasonable expectation of success that modified compounds of Cooper, '485 or '124 would be pharmacologically active at the dopamine D_3 receptor, particularly where the critical moiety of the starting compound, the arylsulfonamide radical, is destroyed through the course of modification. In view of the foregoing, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 1, 2, 6-10 and 12-23 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Cooper, the rejection of claims 1, 2, 6-13 and 15-23 under 35 U.S.C. § 103(a) as allegedly being unpatentable over '485, and the rejection of claims 1, 2, 6-8, 12, 13 and 15-23 under 35 U.S.C. § 103(a) as allegedly being unpatentable over '124.

3. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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